Tech@Breakfast AGENDA

7:30 – 8:00 Networking

7:55 – 8:00 Announcements/Event Calendar

8:00 – 8:35 Panel Presentation

8:40 – 9:00 Discussion & Q & A

The Promise of Personalized Medicine……Utah's Role

A Panel Discussion

Moderator

Ned M. Weinshenker, Ph.D. Director, Life Sciences Cluster, GOED

Panelists

Jerry Lanchbury, Ph.D. *Executive Vice President of Research,* Myriad Genetics

Daryll DeWald, Ph.D. *Associate Director*, Center for Integrated BioSystems (USU)

C. Lars Mouritsen, CLSp(MB). *Chief Scientific Officer*, Sorenson Genomics, Inc.

Kevin Flanigan, M.D. *Adjunct Associate Professor of Human Genetics, (U of U)*

Michael S. Paul, Ph.D., *Chief Operating Officer & President*, LineaGen

Tech@ Breakfast March 24, 2006

Predictive & Personalized Medicine

- **Predictive**- The ability to predict the probability of future health problems based on specific genetic information to:
  - Plan appropriate medical monitoring
  - Administer timely preventative therapies
- **Personalized** -The ability to tailor a therapeutic regimen based on an individual's overall genetic makeup to:
  - Improve efficacy
  - Reduce side effects

Recent Examples of Medical Differences Sex/Ethnic Groups

- **March 2006** -Stryker spotlights new female knee replacement **(**said its knee replacement product specifically designed for females has been implanted in some 30,000 women.)
- **Feb 2006** WSJ- Doctors Focus New Attention On Heart Disease in women
- **June 2006-** NitroMed, Inc. (Nasdaq: NTMD) announced today that the U.S. Food and Drug Administration (FDA) approved BiDil(R) (isosorbide dinitrate/hydralazine hydrochloride) for the treatment of heart failure in black patients.
- **2004** AstraZeneca drug Iressa
  - However, in patients of Oriental origin and in patients who have never smoked the data suggested a statistically significant improvement in overall survival; in the patients of Oriental origin, IRESSA increased median survival by four months.

    AstraZeneca is committed to working to fully understand the results of the ISEL study. Different groups of patients clearly respond differently to IRESSA and by analyzing the full ISEL dataset, we hope to understand more about who responds and why. AstraZeneca is in constructive dialogue with regulatory authorities around the world to ensure that IRESSA remains available for those patients who need it.

The Next Step
Unique Therapies for Individuals

- How do we get there?
- What tools are available today?
- What tools do we need in the future?
- What is the activity currently in Utah companies, Medical Centers and Universities?
- How can Utah entities work together to align resources?
- What resources, if any, are we missing?

Personalized Medicine

CENTER FOR INTEGRATED BIOSYSTEMS

Understanding the molecules and messages of life.

Individual genetic and metabolic information as tools for disease prediction, diagnosis and/or treatment

Daryll DeWald, Ph.D.

Personalized Medicine

CENTER FOR INTEGRATED BIOSYSTEMS

Understanding the molecules and messages of life.

Relevant Research at USU

- Nutrition/Obesity research (UCAN)
- Alzheimer's Disease research (CES)
- Autism (CPD)
- Cancer research (CIB)

Personalized Medicine and Obesity

CENTER FOR INTEGRATED BIOSYSTEMS
Understanding the molecules and messages of life.
Timothy Gilbertson, Ph.D.

Example:

Using genomic and metabolomic information to predict or treat obesity

- **Genomics**

  genetic linkages to obesity-gene chip technologies

  genetic profiles leading to adverse affects from therapeutic intervention

Metabolomics

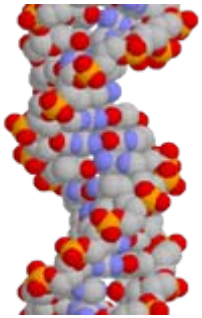
personal metabolome profiles of obesity

adjusting an individuals metabolome for optimum outcomes

PATHWAY TO SUCCESS

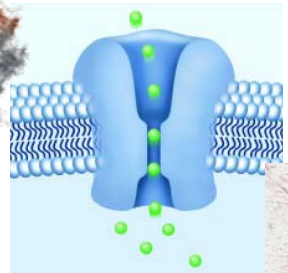
applies to <u>any</u> nutrition-related disorder

gene

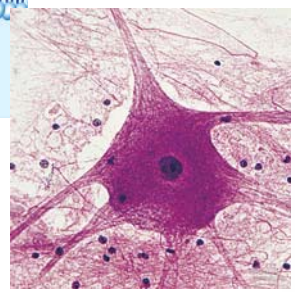


molecule

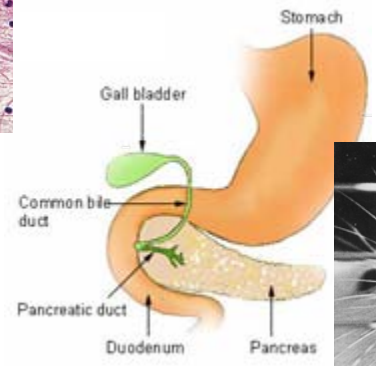
protein



cell



tissue/organ



behavior

treatment

"Utah Center for Advanced Nutrition"

USTAR Utah Science, Technology, and Research Economic Development Initiative

Timothy Gilbertson, Ph.D.

Personalized Medicine Needs

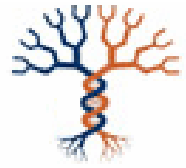
CENTER FOR INTEGRATED BIOSYSTEMS

Understanding the molecules and messages of life.

- **Technological advances-** e.g., personal gene chips, patient scale metabolomic instrumentation
- **Multidisciplinary research centers-** e.g., Autoimmune Disorders Research Center, Center for Genetic Medicine
- **Improvement in data management**
- **Care provider education-** use of genetic information
- **Patient education-** value and challenges of personalized medicine

SorensonGenomics

High-throughput DNA Genotyping and Sequencing



Personalized and Predictive Medicine

Presented by
Lars Mouritsen
March 24, 2006

General Perspectives

- Personalized medicine will be a necessary future requirement to reduce drug failures.
- Drug companies will need to respond appropriately.
- Diagnostics/technology will be required to assist pharma's.
- Accurate family health histories will be required.
- Disease risk assessment will be critical.

SorensonGenomics
High-throughput DNA Genotyping and Sequencing

Utah Perspectives

- Utah strengths
  - USTAR initiative to fund research
  - Genealogical records
  - Genetic research
  - Willing patient population
- Possible weaknesses
  - Focused goals
  - Concerted effort between industry, academia and government.
  - Unified record management system

Technologies

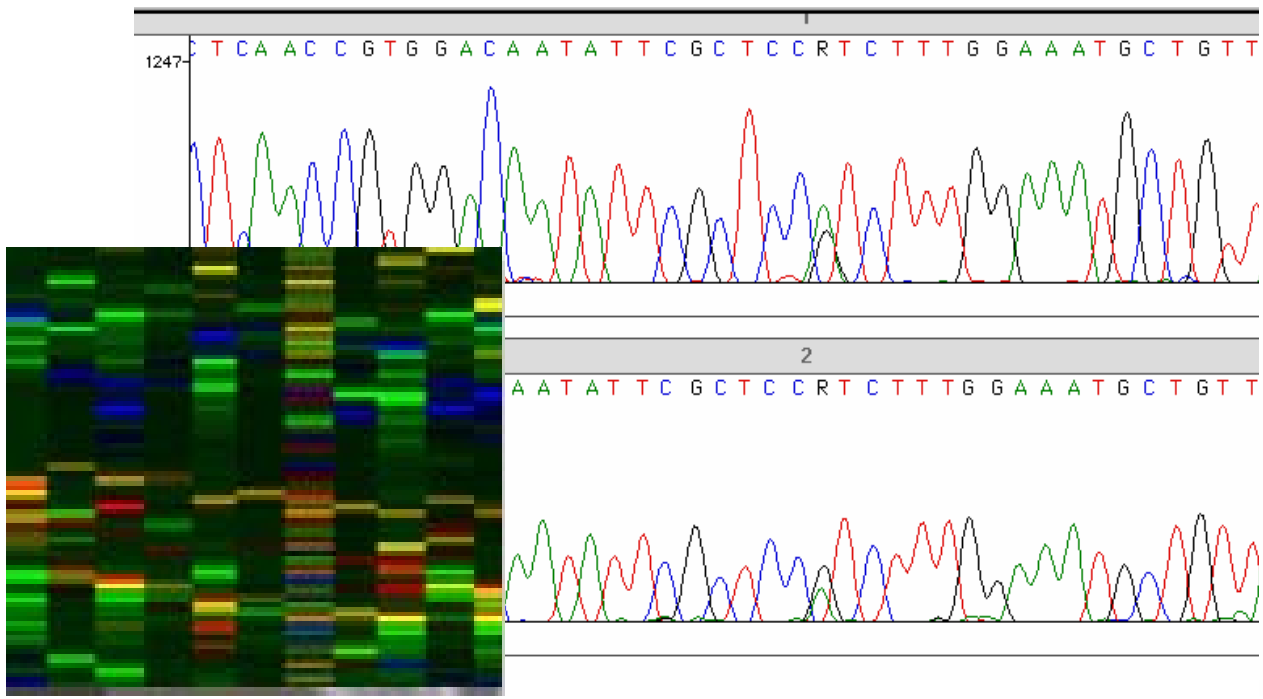
- Whole Genome Sequencing
  - Solexa - **Clonal Single Molecule Array™** technology, allows simultaneous analysis of hundreds of millions of individual molecules.
  - 454 Life Sciences (Roche) - Light emitting sequencing chemistries to produce over 20 million nucleotide bases per five-hour run
  - Helicos – Single Molecule Sequencing by Synthesis
    - Cambridge Massachusetts 2003 venture capital start-up Helicos Biosciences claims that by 2007 Helicos will be selling a machine that will sequence a person's genome for $5000.
  - Harvard Nanopore Group – Probing molecules with nanopores.
  - US Genomics – Single molecule detection without amplification.
- Whole Genome SNP detection
  - Affymetrix – GeneChip microarrays technology
  - Illumina – Bead array technology
  - Combimatrix - integrated circuits contain arrays of microelectrodes that are individually addressable using embedded logic circuitry on the chip

SorensonGenomics
High-throughput DNA Genotyping and Sequencing

Questions

- Costs of personalized medicine
- How to unify as a state
- How to unify nationally
- How to unify record management
- How to handle and make sense of the data
- Clinician and patient education

Sorenson Genomics

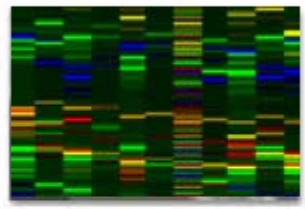


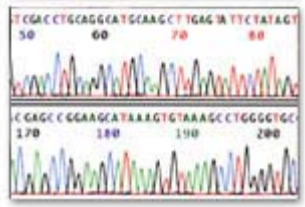
Industry leader of high-throughput genomic testing services for verifying ***human identity*** and ***familial relationships***

SorensonGenomics

High-throughput DNA Genotyping and Sequencing

Areas of Expertise





- Accredited laboratory
- Specimen Processing/Data entry
- Nucleic acid extraction/purification
- Robotics and automation
- Multiplex PCR
- DNA Sequencing
- DNA Genotyping
- Bioinformatics
- Ties to and experience with genetic genealogy (SMGF) database

SorensonGenomics

High-throughput DNA Genotyping and Sequencing

SorensonGenomics

High-throughput DNA Genotyping and Sequencing

Thank you

Human Genetics in Utah: Unique Patient Resources

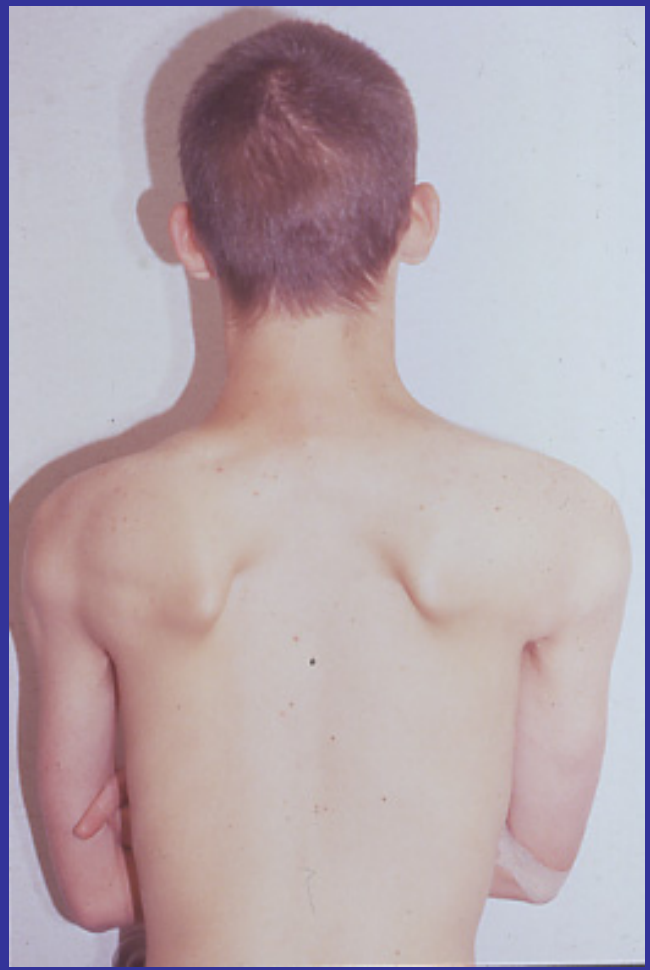
Kevin M. Flanigan, M.D.

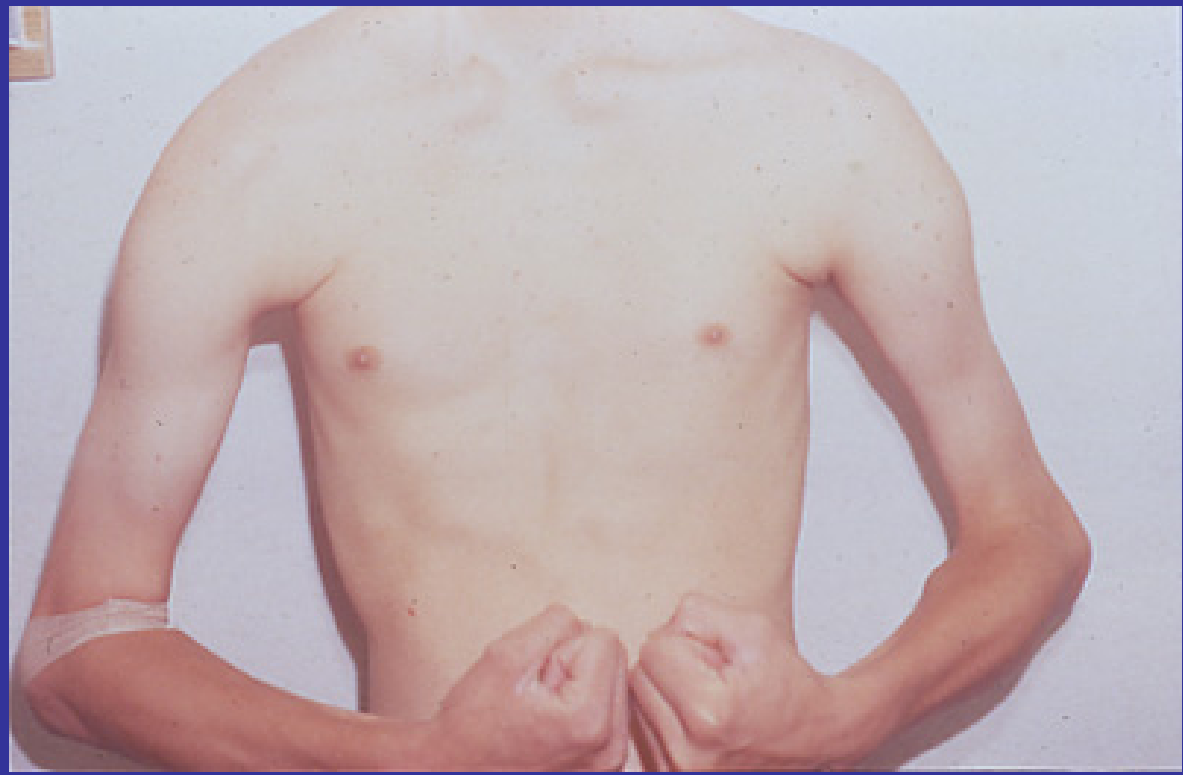
Departments of Neurology, Human Genetics, Pathology, and Pediatrics

University of Utah School of Medicine

"The intermountain area presents an unique opportunity for the study of human inheritance. Although the total population is not great, it is unusual in that the family groups are, in general, large. In the early days of the area, which is only 100 years old in terms of a stable Caucasian population, many polygamous marriages occurred which extended further the number of descendants of a given individual. Because the population is relatively stable a high proportion is available for study. Furthermore, the Church of Jesus Christ of Latter-Day Saints has fostered the keeping of detailed genealogical records from which accurate and complete pedigrees can be constructed."

Tyler FH, Wintrobe MM. Studies in disorders of muscle. I. The problem of progressive muscular dystrophy. Ann Intern Med 1950;32:72-79.





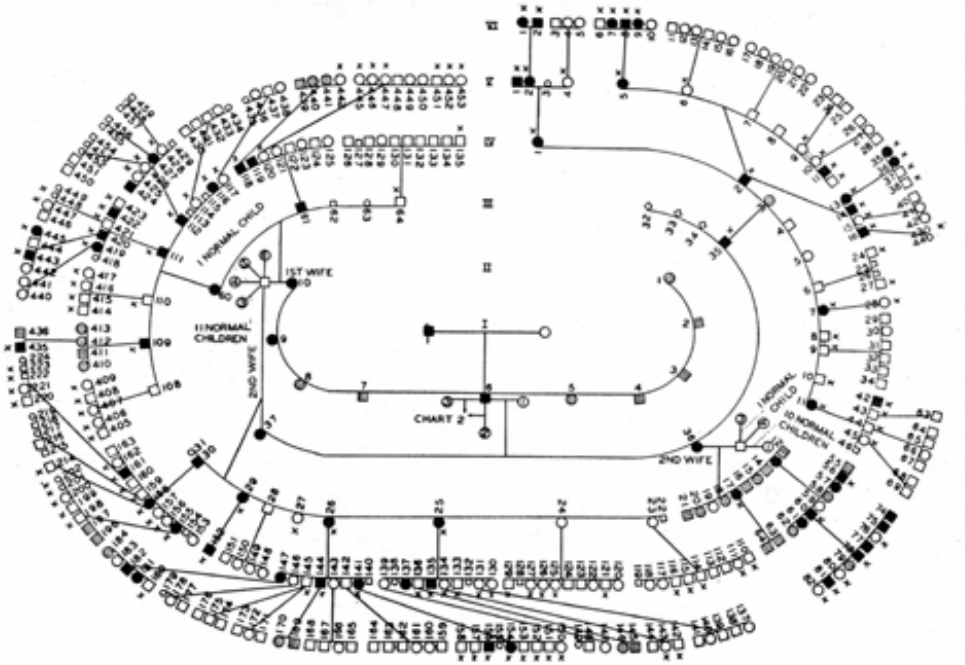


FIG. 1. Pedigree of kindred. The descendants of II-6 by his second and third wives are diagrammed separately in figure 2.

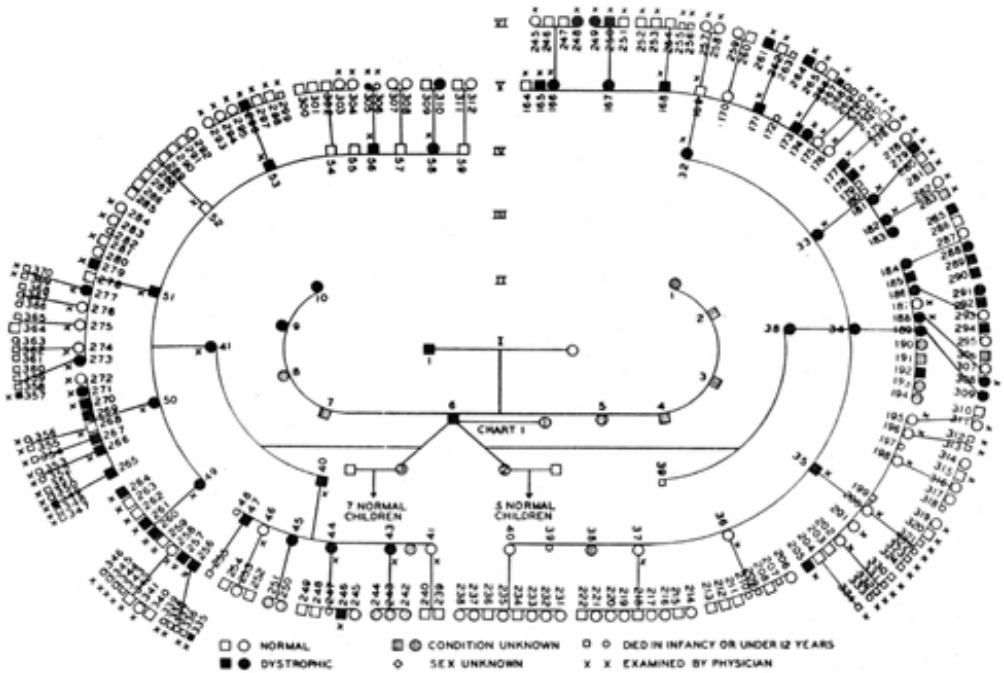
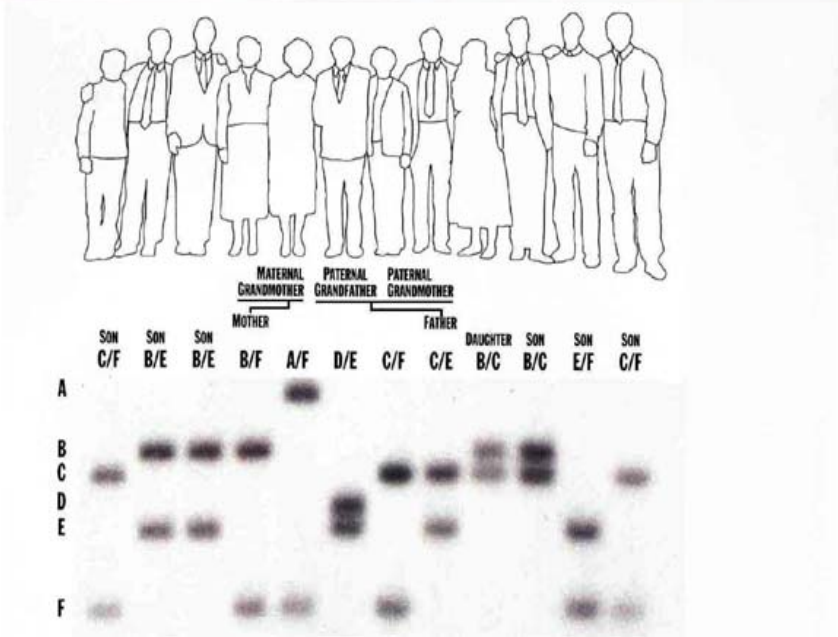


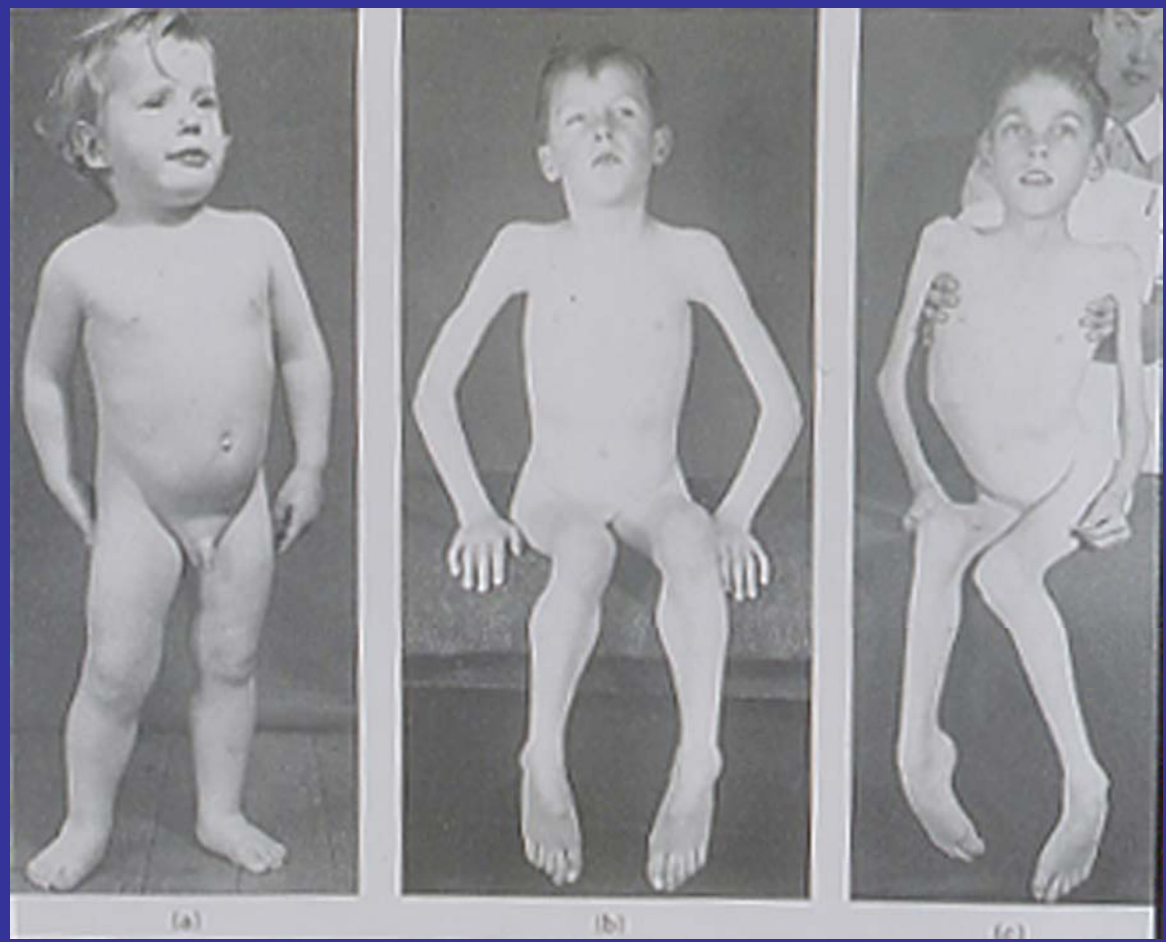
FIG. 2.


MATERNAL GRANDMOTHER
PATERNAL GRANDFATHER
PATERNAL GRANDMOTHER
MOTHER
FATHER
SON C/F
SON B/E
SON B/E
B/F
A/F
D/E
C/F
C/E
DAUGHTER B/C
SON B/C
SON E/F
SON C/F
A
B
C
D
E
F

Utah offers unique resources to study genetic traits

- Unique patient resources
  - Families (size; records; cooperation)
  - Utah Population Database
- World-class phenotypic analysis
  - Clinically
  - Radiographically
- Genetics expertise
  - Core facilities and collaborators with experience/equipment from the Human Genome Project, HapMap, and large association studies
  - Long record of success in mapping disease genes in neurologic disease, cancer, heart disease and more

Personalized Medicine: Mutation-specific therapies for Duchenne Muscular Dystrophy



Am. J. Hum. Genet. 72:931–939, 2003

Rapid Direct Sequence Analysis of the Dystrophin Gene

Kevin M. Flanigan,[1,2,3,4] Andrew von Niederhausern,[2] Diane M. Dunn,[2] Jonathan Alder,[2] Jerry R. Mendell,[5] and Robert B. Weiss[2]

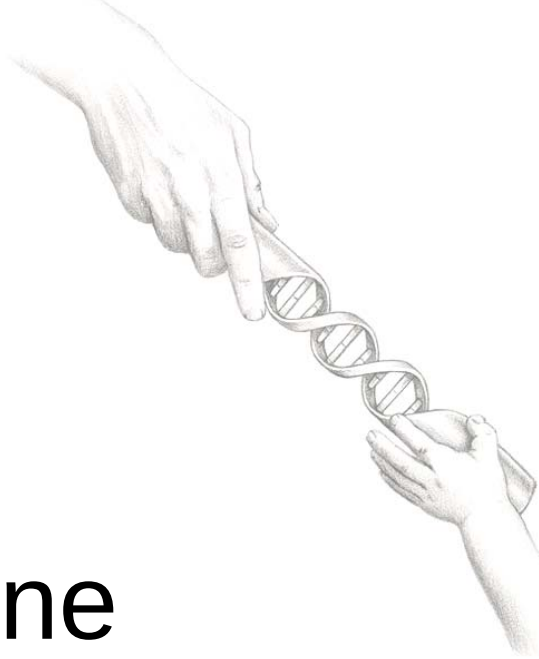
Departments of [1]Neurology, [2]Human Genetics, [3]Pathology, and [4]Pediatrics, University of Utah, Salt Lake City, and [5]Department of Neurology, Ohio State University, Columbus

Mutation-specific therapeutic trials at the University of Utah

- Premature stop codon readthrough (trials in progress)
  - NIH
  - PTC Therapeutics, Inc. (novel compound)
- Exon skipping (planning)
- Gene transfer (planning)

Summary

- Utah families represent unique resources
- Utah researchers have long experience in using patient resources to advance medical knowledge
- This knowledge is now being translated back into clinical trials of potential benefit to Utah citizens

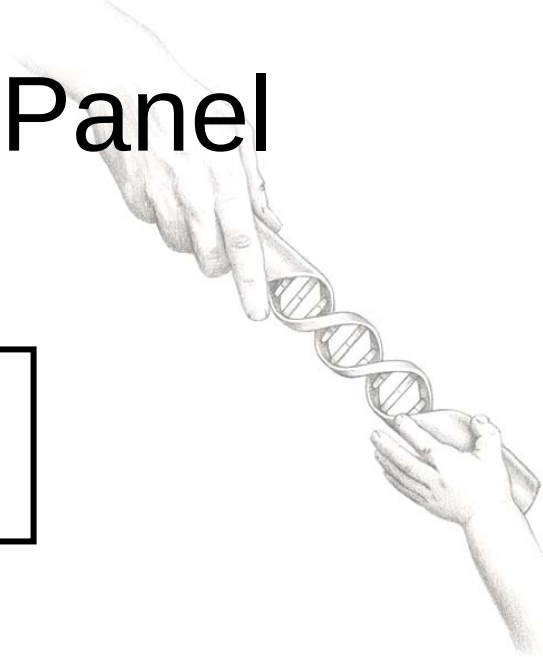


Tech@Breakfast
Personalized Medicine

Michael Paul

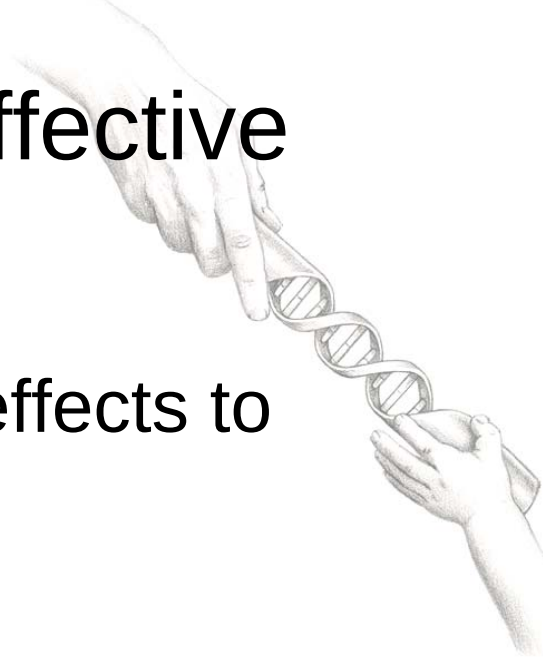
March 24, 2006

Personalized Medicine Panel Topics



- View of Personalized Medicine
- What does Utah have to offer?
- How is LineaGen contributing?
- What is needed for further success?

Bottom-line…safer/more effective medicines



- Each year in the United States side effects to medications cause:
  - Over 100,000 deaths
  - More than 2 million hospitalizations
- The effectiveness of prescribed medications ranges from 20-60%
- Medicines are developed for the “average” person

With new tests, we could markedly improve any existing medication — ensuring it would help everyone who took it, and decreasing the likelihood of side effects

And, There Already Are Tests For Sale on the Internet!

Personal Business

Genetic Predictions: Just a Swab Away

By NAOMI FREUNDLICH

PETER DYCK, a retired electrician from Portland, Ore., previously took seven medications to treat his congestive heart failure and other maladies, but the regimen brought no major improvement. In fact, during that time, he developed a debilitating cough that kept him up at night and often left him gasping for air during the day.

His doctors were baffled. "I had been fighting with this coughing thing for over half a year," said Mr. Dyck, 51. Specialists first suspected tuberculosis, then treated him for asthma, he said.

His family, though, wondered whether his medications might be at fault. At the urging of his daughter, Sarah Knell, Mr. Dyck said, he took a new genetic test, sold online through **Genelex** of Seattle, that promised to shed some light on how his body metabolizes drugs. After taking the test — he swabbed the inside of his cheek with a device like a large Q-Tip and sent the specimen to a laboratory for analysis — he learned that his liver was slow in breaking down certain chemicals. That meant that some drugs, including one of his heart medications, could easily build up in his system, decreasing their effectiveness and causing side effects.

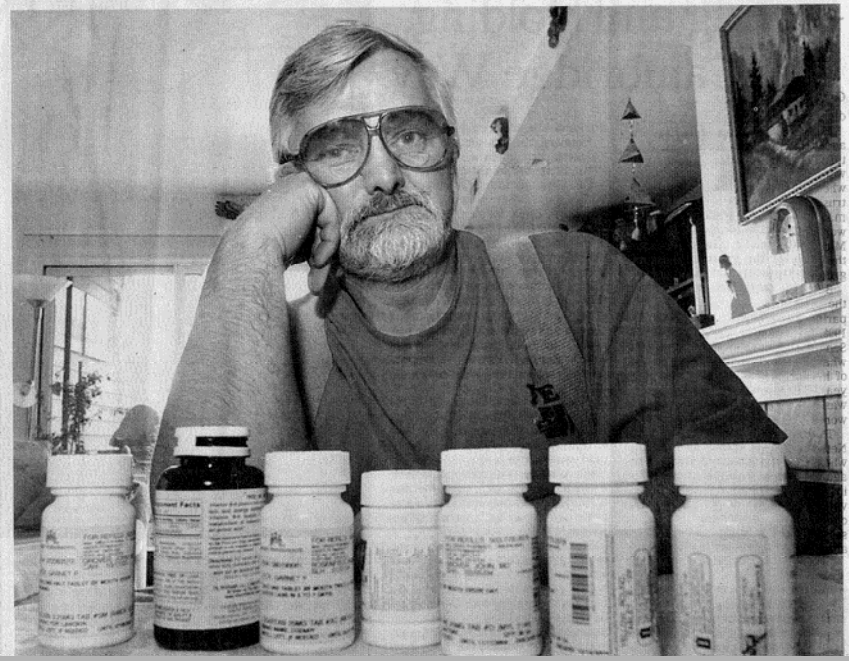
Mr. Dyck said he had taken the results of the test, which sells for $500 to $600, to his doctors, and they modified his medications

companies promise that the results will remain confidential.

Just how reliable are these tests? Most genetic tests marketed directly to consumers are for common gene variations linked to an increased risk of certain illnesses. They can sometimes indicate whether someone is more susceptible than others to a particular disease, but they cannot predict with certainty that the disease will develop, according to the companies that sell them.

Medical experts worry about the relevance of the tests, and about consumers' ability to interpret the lab results accurately. "It can be harmful when people have inaccurate assumptions or expectations about their future health," said Jonathan Zonana, a professor of molecular and medical genetics at the Oregon Health and Science University in Portland. Some companies, like Genelex and **Genova Diagnostics** of Asheville, N.C., which sells tests under the names Genovations and Great Smokies Diagnostic, run batteries of genetic tests and provide customers with the results, along with suggestions on how to make lifestyle changes to help reduce disease risk. (Though marketed to consumers, the Genovations tests are available only through doctors and other health care providers like acupuncturists.)

Genelex and Genova do not bill their tests as having all the answers, but rather as aids for preventing diseases when used with information about family histories and lifestyle factors. Genovations' heart disease ge-



- Unfortunately, we don't have all the tests we need to make this vision a reality; and
- More will have to be discovered (new content)

man Genome Project. The project, publicly

evaluation and safety for the F.D.A., said

dysfunction. In each area, the tests looks for

ence. "You may be misleading people, nav-

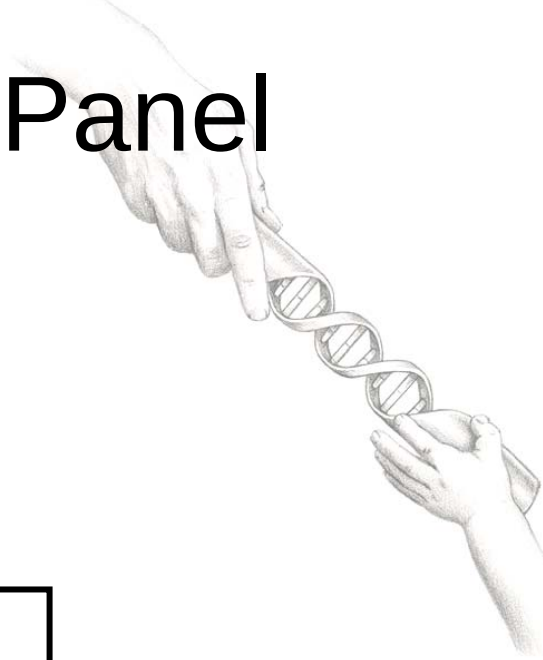
UT what about patients who do test

Discovery of new content is key driver

Best in class technology is readily available

AmpliChip CYP450 Test

Personalized Medicine Panel Topics



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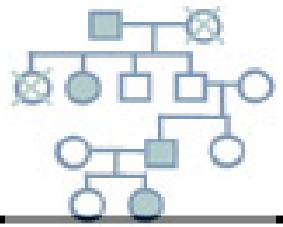
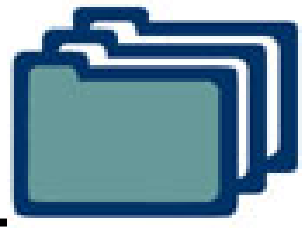
What Does Utah Have to Offer for This New Approach?

- Both responsiveness to medications and the risk of side effects depend on:
  - Our individual genetic makeup
  - How our genes interact with our life experiences (such as the medications we take)

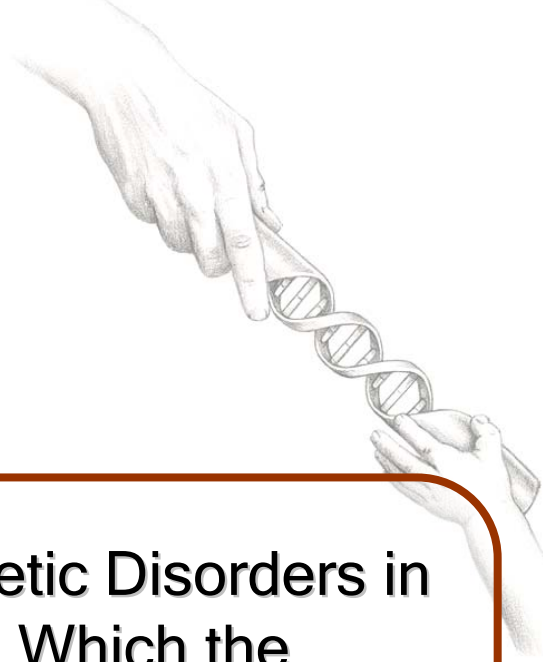
There is no other place in the United States where we can understand the genetic structure of the population

Integrated Personalized Medicine Content

Genealogy-Based Population Records	Comprehensive Medical Records	Patient -Oriented Research Clinics
		

Unmatched Biomarker Discovery Platform

Inherited Disorder	Gene
Colon Cancer (Familial Adenomatous Polyposis Coli)	*APC*
Neurofibromatosis	*NF-1*
Breast Cancer	*BRCA-1*
	BRCA-2
Melanoma	*p16*
Cardiac arrhythmias (Long QT Syndrome)	*KVLQT1*
	minK
	HERG
	MiRP1
Supravalvular Aortic Stenosis	*ELN*
Alport Syndrome	*COL45A5*
Hypertension	*XIB*
	AGT
Macular degeneration (Stargardt's Disease)	*ABCR*
Ulnar-Mammary Syndrome	*TBX3*
Williams Syndrome	*LIMK1*
Porphyria Cutanea Tarda	*URO-D*
Inflammatory Syndromes	*PAF-AH*
Chediak-Higashi Syndrome	*CHS-1*
Neonatal Epilepsy	*KCNQ2*
	KCNQ3
Hyperkalemic Periodic Paralysis	*SCN4A*
Paramyotonia Congenita	*SCN4A*
Potassium Aggravated Myotonia	*SCN4A*
Hypokalemic Periodic Paralysis	*CACNA1S*
Periodic Paralysis 3	*KCNE3*
Andersen's Syndrome	*KCNJ2*
Frings Audiogenic Epilepsy	*Mass1*
Spinocerebellar Ataxia Type 7	*SCA7*
Familial Advanced Sleep Phase Syndrome	*hPer2*

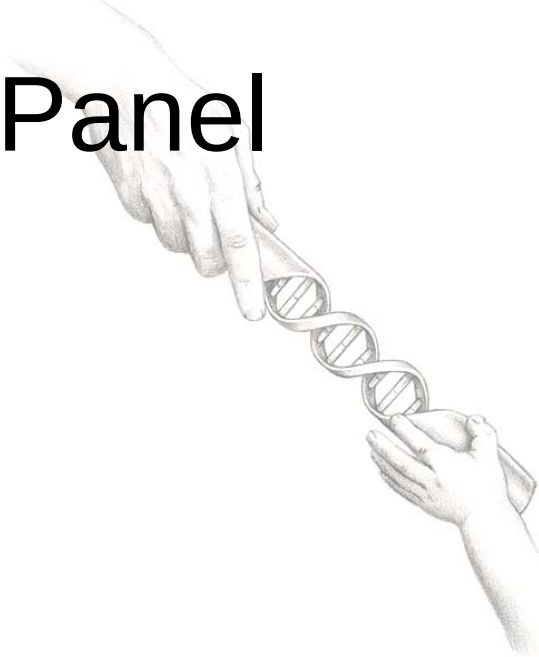


Genetic Disorders in Which the Molecular Basis Was Discovered at the University of Utah

Why genetics is important to understand

Disease	# of Deaths*	Genetic Susceptibility?
Heart Disease	696,947	Yes
Cancer	557,271	Yes
Stroke	162,672	Yes
Lower Respiratory Disease	124,816	Yes
Adverse Drug Reactions (est)	106,000	Yes
Diabetes	73,249	Yes

Personalized Medicine Panel Topics



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Mission: "Commercialize Utah's Core Genetic Assets"

LINEAGEN RESEARCH CORPORATION

- Corporate Partners
- Spin-out Companies

Bringing partners to Utah…

LINEAGEN RESEARCH CORPORATION

AMGEN®

IBM®

CELERA DIAGNOSTICS
A Joint Venture With Applied Biosystems

Bristol-Myers Squibb Company

MERCK

Battelle

MERRIMACK PHARMACEUTICALS

…and partnerships bring recognition

LINEAGEN RESEARCH CORPORATION

IBM®

DESERET Morning News
deseretnews.com salt lake city, utah

AP Associated Press

washingtonpost.com

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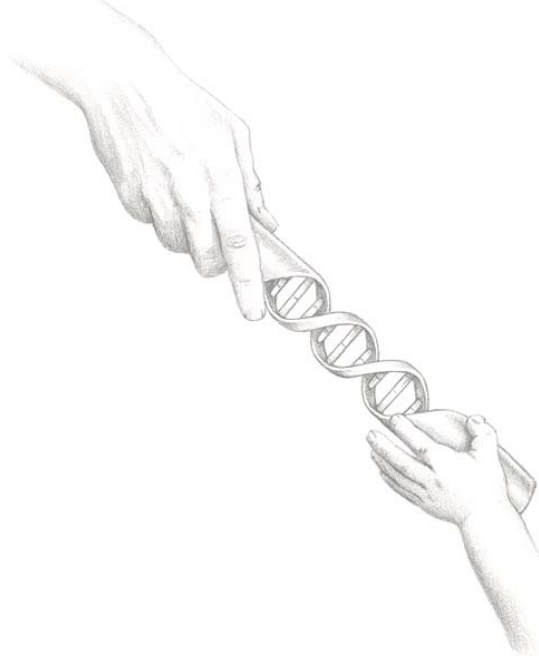
THURSDAY SEPTEMBER 16, 2004 — THE DAILY BIOTECHNOLOGY NEWSPAPER — VOLUME 15, NO. 179 PAGE 1 OF 6

Next Steps



LINEAGEN RESEARCH CORPORATION

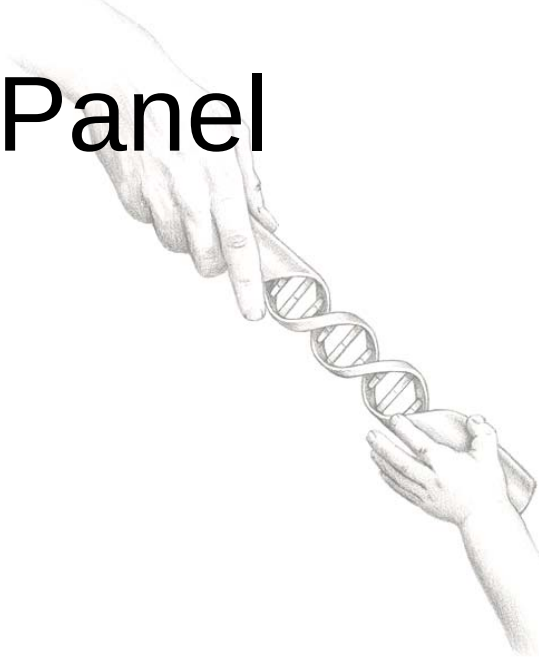
RESPIRIS

- Utah start-up focused on respiratory biomarkers
- D_x and R_x utility
- Late-stage negotiations on $xxMs collaboration

LINEAGEN PARTNERS INC.

- Commercialization Fund
- Novel financing model
  - $50M - $75M
- Returns via strategic licensing of biomarker IP

Personalized Medicine Panel Topics



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What is needed…a new game

- Big problems with biotech financing model
  - big funds force a later stage focus
  - early stage VC investing declining or very flat
  - inhibits vs. enables innovation

- Proposed solutions
  - novel investment model/s
  - commercialization of projects, not companies
  - rigorous project management “framework”
    - proof-of-concept with lower operating costs

Contact Information

Web-site: **www.goed.utah.gov**

Blog: **www.goed.utah.gov/clusters**

nweinshenker@utah.gov

Next Month's Technology@Breakfast

Friday, April 28

Questions?

Governor's Office of Economic Development